

Appl. No. 09/631,339
Reply to Final Office Action of June 22, 2006

REMARKS

On August 17, 2006, Applicants submitted a response to the final rejection of the claims, mailed June 22, 2006. In an Advisory Action dated September 5, 2006 the Examiner stated that the claim amendments submitted in the August 17, 2006 response would not be entered as they raised new issues. Applicants submit herewith a Request for an RCE and an accompanying Amendment and Reply. Applicants request that the previously non-entered amendments submitted on August 17, 2006 not be entered. Instead, applicants request entry of the claim amendments submitted herewith in place of the August 17, 2006 submitted claim amendments.

Claims 1 and 23 have been amended to specify the inner diameter of reaction portion of applicants' claimed device. Support for the amendment is found on page 19, lines 15-17. Claim 4 has been amended to incorporate the limitation of claim 12, and claims 12 and 24 have been amended to correct typographical errors. New claim 25 specifies the length of the capillary tube portion. Support for that amendment is found on page 17, lines 16-19.

Claim 24 was objected to for depending from a canceled claim. Applicants have amended claim 24 to properly depend from claim 23. The amendment is believed fully responsive to the Examiner's request for correction, and applicants respectfully request entry of that amendment.

Claims 1-3, 5, 6, 9-11, 15, 23 and 24 stand rejected under 35 USC 103 as being unpatentable over von Behrens (US 3,914,985) in view of Fite et al (US 5,142,143). Applicants respectfully traverse.

The von Behrens reference is directed to a centrifuge device for use in harvesting, compacting and measuring particulate matter in liquids such as blood and other body fluids. The device overcomes previous difficulties in estimating the total volume percent of thrombocytes, lymphocytes and granulocytes in blood, by compacting the components of

Appl. No. 09/631,339
Reply to Final Office Action of June 22, 2006

blood (or other body fluid) in the disclosed centrifuge device. The von Behrens device comprises a capillary tube portion attached to a larger upper section wherein the capillary section can be formed of glass or other rigid plastic (see column 4, lines 33-35). Optionally the lower end of the capillary section is permanently sealed (column 5, lines 64-65). There is no suggestion anywhere within von Behrens regarding heating the device or optically interrogating the device contents through the end of the device.

The present invention is directed to a container comprising a capillary tube, closed at one end, that is used for rapid thermally cycling a sample added to the container. The desirability of rapidly and homogeneously heating and cooling the contents of the container has led to applicants' invention which requires 1) that the container be prepared from materials having a high thermal conductivity, 2) that the container walls be thin to enhance thermal transfer between the interior of the container and the exterior environment and 3) that the diameter of the capillary tube be of sufficiently narrow dimensions to provide a high surface area to volume ratio for the sample contained in the container. The von Behrens reference fails to teach or suggest a container having the physical properties of applicants' device, due in part to the fact that the von Behrens device is intended for an entirely different purpose than applicants' device.

The Examiner contends that the recited thermal conductivity of the reaction portion of applicants' device is met by the fact that von Behrens discloses their device can be made of glass. However, applicants note that glass is only one of the materials suggested for constructing the von Behrens device. "[O]ther transparent materials such as rigid plastics..." are also suggested as suitable materials for the von Behrens device. Since von Behrens fails to cite any desirability with regards to thermal conductivity, von Behrens fails to provide any motivation for selecting glass as the material used for their device, provided the alternative material provides sufficient dimensional control during formation of the device.

Appl. No. 09/631,339
Reply to Final Office Action of June 22, 2006

Furthermore, von Behrens note that "the lower capillary tube section 12b is relatively fragile, at least where glass is used in its fabrication..." (emphasis added), again suggesting that materials other than glass can be used, and actually providing expressed motivation to one skilled in the art to use materials other than glass.

The claims of the present invention further specify that the capillary tube portion is closed at one end, and in one embodiment is closed in a manner that allows for optical transmissibility through the closed end. The Examiner contends that since glass is one material that can be used to form the capillary section of the von Behrens device, the "sealed end" of the von Behren device is also made of glass. However the von Behrens' disclosure simply states that the capillary section "may be permanently sealed" without specifying how the end is sealed or the material used to seal the end. There are many ways of sealing an open end of a capillary tube, and von Behrens provides no guidance on how the end is sealed, or that the end should be sealed in a manner that allows optical transmissibility through the "sealed" end. The Examiner contends that Fig. 6 demonstrates that the sealed end is formed from the same material as the walls of the capillary tube, however there is no text that supports the Examiner's position and furthermore, as noted above, the von Behrens disclosure does not require the use of glass to form the capillary tube portion of the device.

As acknowledged by the Examiner, von Behrens also fails to teach or suggest a device comprising a thin walled capillary section of about 0.1 in thickness. To overcome this acknowledged deficiency of the von Behrens reference, the Examiner has cited the secondary reference, Fite (US Patent No. 5,142,143) as demonstrating that capillary tubes having a wall thickness of about 0.1 were known in the art. Applicants do not dispute that such open ended capillary tubes existed in the prior art. However, as applicants demonstrated in their Response filed on April 19, 2006 (see Exhibits A-D) many capillary tubes of differing wall thicknesses were also publicly available at the time of applications' invention. The Examiner

Appl. No. 09/631,339

Reply to Final Office Action of June 22, 2006

has failed to provide any reasoning why one of ordinary skill would modify the device of von Behrens to include a capillary tube having the wall thickness of the capillary tube disclosed in Fite. In this regard it is important to note that the capillary tube disclosed in Fite cannot simply be used to substitute for the capillary portion of the device disclosed in von Behrens to reconstruct the presently claimed container. The capillary tube disclosed in Fite is open at each end (as required to allow gas to flow through the sorbent filled capillary) and has a larger inner diameter than applicants' device.

Applicants' claimed device requires a capillary that is closed at one end in a manner that allows optical transmissibility through the closed end. Furthermore, to optimize rapid and uniform temperature modulation of a sample, the container has a narrow inner diameter selected from the range of 0.25 mm to 1.0 mm. The capillary tube cited in the Fite reference has a diameter 50% larger than the maximum diameter allowed by applicants' claimed device. This difference in the inner diameter of the Fite capillary and the capillary portion of the present invention results in the Fite capillary providing a substantially decreased volume to surface area ratio relative to the presently claimed capillary portion of applicants' device. Specifically, the volume to surface area ratio is at least 30% less than the ratio of applicants' claimed capillary portion (surface area = $2\pi(r)h + 2\pi r^2$; Fite surface area = 177.9, our device with $r = 1.0$ and height 80mm has a surface area = 252.8; volume = $\pi r^2 h$; with total Fite capillary volume = 65mm^3 , and total volume for the claimed capillary portion = 63mm^3 , wherein the: volume to surface area ratio is about 0.36 for the Fite capillary and about 0.25 for the presently claimed capillary portion). Accordingly, the capillary tube disclosed in Fite cannot simply be substituted for the capillary portion of the von Behrens device to recreate applicants' claimed sample container. To reconstruct applicants presently claimed invention, the Examiner is selecting one feature of one capillary tube disclosed by Fite (i.e., the thin

Appl. No. 09/631,339
Reply to Final Office Action of June 22, 2006

walls of 0.1mm) without providing any motivation for selecting this one element from one of many different capillary tubes that were commercially available.

Applicants respectfully submit that obvious to try is not the legal standard for obviousness. The von Behrens reference discloses numerous components of their device that can be varied. The prior art is replete with capillary tubes of different dimensions. The Examiner has failed to provide motivation for selecting the specific variables he recites from von Behrens, for combination with one specific element from one specific capillary from the many different types commercially available. Applicants' designed their container based on the desire for rapid, uniform heating and cooling of a sample, the cited references are devoid of any suggestion of the desirability for such rapid heating and cooling of a sample and therefore provide no motivation to make the combination advanced by the Examiner.

The fact that the presently claimed invention discloses and claims a combination of features previously disclosed in separate devices is not fatal to patentability. A basic issue is whether the applied references, alone or in any combination, suggest the claimed invention as a solution to the specific problem solved. This is particularly relevant in the present situation wherein the prior art reference is directed to solving a different problem, and functions in a manner completely unrelated to the presently claimed invention. When the prior art itself does not suggest or render "obvious" the claimed solution to that problem, the art does not satisfy the criteria of 35 USC § 103 for precluding patentability. *Lindemann Maschinenfabrik GmbH v. American Hoist and Derrick Co.*, 730 F2d 1452 (Fed Cir 1984).

Applicants have disclosed and narrowly claimed a sample container that is designed to provide for optimal rapid thermal cycling of the sample contents. The Examiner has selected various elements from the cited art reference (glass vs "other transparent materials", sealing the end with glass vs other art recognized materials and methods, and selection of one feature of one particular capillary tube from a wide variety of commercially available

Appl. No. 09/631,339
Reply to Final Office Action of June 22, 2006

products) in an attempt to reconstitute applicants' claimed invention. However, applicants note that even if one accepts such a combination was proper, which applicants do not, the combination still fails to regenerate applicants' claimed invention because the Fite capillary is too wide and provides a less optimal surface area to allow rapid and uniform heating and cooling of the sample. When prior art references require a selective combination and further modification to render obvious a subsequent invention, there must be some reason for the combination other than the hindsight gleaned from the invention itself. It is impermissible to use the claims as a frame and the prior art references as a mosaic to piece together a facsimile of the claimed invention. *Uniroyal Inc. v. Rudkin-Wiley Corp.*, 837 f2d 1044 (Fed Cir 1988).

The Examiner states that in the absence of a showing of criticality and/or unexpected results, it would have been obvious to modify the von Behrens device to include the capillary tube disclosed in Fite and to seal the end of that capillary in a manner that allows for optical transmissibility. Applicants respectfully submit they are not required to provide a showing of criticality and/or unexpected results when the Examiner has merely made a conclusory statement of obvious and has failed to establish a prima facie case of obviousness. The Examiner bears the initial burden of factually supporting any prima facie conclusion of obviousness (MPEP 2142), and applicants respectfully submit that the Examiner has failed to meet this initial burden. The Examiner has failed to meet his burden due to the lack of motivation for selecting one feature of one capillary tube disclosed in Fite from all the other capillary tubes that are commercially available for combination with selected features of the von Behrens disclosure.

When patentability turns on the question of obviousness, the search for and analysis of the prior art includes evidence relevant to the finding of whether there is a teaching, motivation, or suggestion to select and combine the references relied on as evidence of obviousness. See, e.g., *McGinley v. Franklin Sports, Inc.*, 262 F.3d 1339, 1351-52, 60

Appl. No. 09/631,339
Reply to Final Office Action of June 22, 2006

USPQ2d 1001, 1008 (Fed. Cir. 2001) ("the central question is whether there is reason to combine [the] references," a question of fact drawing on the Graham factors).

"The factual inquiry whether to combine references must be thorough and searching."
Id. It must be based on objective evidence of record. This precedent has been reinforced in myriad decisions, and cannot be dispensed with. See, e.g., *Brown & Williamson Tobacco Corp. v. Philip Morris Inc.*, 229 F.3d 1120, 1124-25, 56 USPQ2d 1456, 1459 (Fed. Cir. 2000) ("a showing of a suggestion, teaching, or motivation to combine the prior art references is an 'essential component of an obviousness holding'" (quoting *C.R. Bard, Inc., v. M3 Systems, Inc.*, 157 F.3d 1340, 1352, 48 USPQ2d 1225, 1232 (Fed. Cir. 1998)); *In re Dembiczak*, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999) ("Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references."); *In re Dance*, 160 F.3d 1339, 1343, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998) (there must be some motivation, suggestion, or teaching of the desirability of making the specific combination that was made by the applicant); *In re Fine*, 837 F.2d 1071, 1075, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988) ("teachings of references can be combined only if there is some suggestion or incentive to do so.") quoting *ACS Hosp. Sys., Inc. v. Montefiore Hosp.*, 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed. Cir. 1984).

The need for specificity pervades this authority. See, e.g., *In re Kotzab*, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000) ("particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed"); *In re Rouffet*, 149 F.3d 1350, 1359, 47 USPQ2d 1453, 1459 (Fed. Cir. 1998) ("even when the level of skill in the art is high, the Board must identify specifically the principle, known to one of ordinary skill that

Appl. No. 09/631,339
Reply to Final Office Action of June 22, 2006

suggests the claimed combination. In other words, the Board must explain the reasons one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious."); *In re Fritch*, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) (the examiner can satisfy the burden of showing obviousness of the combination "only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references").

The von Behrens device is directed to a container suitable for use in centrifuging and compacting particulate matter in a liquid sample. This reference fails to provide any motivation for modifying the device to optimized rapid thermal cycling of the container's contents. The Examiner has stated that rapid heat control is one of the factors that would motivate one to modify the von Behren device for performing "microhematocrit operations that require temperature control." However, there is simply no suggestion within von Behrens of such "temperature control operations" or of any need to rapidly cycle the temperature of the microhatocrit contents. Applicants are not aware of any "microhematocrit operations" that would require rapid heating and cooling of a sample, and invite the Examiner to support his statement with an actual example.

There is simply no objective reason provided by the Examiner why a microhematocrit tube should be formed to allow rapid thermal cycling of its contents. When a patent Examiner relies on what they assert to be general knowledge to negate patentability, that knowledge must be articulated and placed on the record. *In Re Sang Su Lee*, 277 F.3d 1338 (Fed. Cir. 2002). The known properties of an element (i.e. that thin walled capillaries will allow rapid heating and cooling of the capillary space) cannot serve as motivation for combining that element with a prior art device absent some objective reason why the known property would be advantageous in a device resulting from such a combination.

Appl. No. 09/631,339
Reply to Final Office Action of June 22, 2006

The secondary reference, Fite, is directed to a preconcentrator for analyzing trace constituents in gases wherein a sample gas is introduced to a confined sorbent. In one embodiment, Fite discloses the sorbent can be packed into open ended capillary tubes. Since the Fite reference is limited to the analysis of gases, this reference also fails to provide any motivation for modifying a centrifugation device to include thin walls of about 0.1 mm in thickness. Accordingly, there is no motivation to combine the teaching of Fite (or one particular element disclosed in one embodiment of that reference) with the device disclosed by von Behrens. Nor is there any rationale presented for further modifying the Fite capillary to provide a capillary having an inner diameter of about 0.25 mm to about 1.0 mm.

Furthermore, not only does the Examiner fail to provide any motivation for his selective combination and modification of a single capillary disclosed in Fite (when the prior art is replete with capillary tube having different dimensions) with the device of von Behren, but von Behren suggests that thicker walled capillaries may be desirable to reduce breakage of the device. Von Behrens makes repeated references as to the fragile nature of their inner tube (see for example, column 3, line 5, column 4, lines 67-68). Accordingly applicants respectfully submit that von Behrens is not entirely silent regarding the wall thickness of their capillary tubes as the Examiner contends. Von Behrens' statements regarding the fragile nature of the capillaries provides a direct incentive for using stronger capillary tubes. On the contrary there is incentive provided by von Behrens for using a very thin walled capillary, having walls about 0.1 mm thick in combination with the von Behrens device. Absent an objective reason for selecting a thin walled tube, the von Behrens objective statements encourage one to use stronger (i.e., thicker walled) capillary tubes and thus von Behrens actually teaches away from applicants' claimed container.

The thickness of the capillary walls, the volume to surface area ratio, and the material comprising the container, have a direct bearing on the functionality of the presently claimed

Appl. No. 09/631,339
Reply to Final Office Action of June 22, 2006

containers, which are designed for use in rapid thermal cycling reactions. Accordingly, the claimed containers of the present invention represent a unique combination of elements that allows for optimal rapid thermal cycling of a sample placed within the container. The motivation for combining these separate and distinct elements to form applicants' novel container derives from applicants' discovery of the advantages of conducting rapid, uniform thermal cycling. Prior to that discovery there was simply no motivation to prepare the empty containers of the present invention having a capillary portion with capillary walls only 0.1 mm thick, an inner diameter of about 0.25 mm to about 1.0 mm, and a closed end wherein the closed end is optically transmissible.

The Examiner has failed to provide sufficient motivation for why one would select glass over other transparent material, seal the end in a manner that allows optically transmissibility, and incorporate a capillary tube having a closed, a wall thickness of about 0.1 mm and an inner diameter of about 0.25 mm to about 1.0 mm, when none of those specific elements are required for the functioning of the von Behrens device. It is improper for an Examiner to selectively pick and choose elements from the prior art to arrive at the claimed invention absent a convincing line of reasoning as to why such a selection would have been obvious. Ex parte Clapp, 227 USPQ 972 (BPAI 1985). Accordingly, applicants respectfully submit the Examiner has failed to establish a prima facie case of obviousness.

Therefore, applicants respectfully request the withdrawal of the rejection of claims 1-3, 5, 6, 9-11, 15, 21 and 22 for obviousness under 35 USC 103.

Claim 4 stands rejected under 35 USC 103 as being unpatentable over von Behrens (US 3,914,985) in view of Fite et al (US 5,142,143) taken further in view of Gerarde (US 3,518,804). Applicants respectfully traverse.

Claim 4 includes all the limitation of independent claim 1 and therefore the subject matter of this claim is patentable over the disclosures of von Behrens and Fite for the reasons

Appl. No. 09/631,339
Reply to Final Office Action of June 22, 2006

stated above. The Gerarde reference fails to supplement the inadequacies of the von Behrens and Fite references as described above. Gerarde is directed to a capillary fill device. The invention of claim 4 includes an empty capillary tube that has a closed end formed as a flat tip, and a stopper removably inserted into the receiving portion of the container. The cited references fail to teach or suggest this novel combination of elements. The container of claim 4 is believed to be patentable over the cited combination of references and applicants respectfully request the withdrawal of the rejection of claim 4 for obviousness.

Claims 12 and 20 stands rejected under 35 USC 103 as being unpatentable over von Behrens (US 3,914,985) in view of Fite et al (US 5,142,143) taken further in view of Hawes (US 3,556,659). Applicants respectfully traverse.

The inadequacies of the von Behrens and Fite teachings have been discussed previously. In addition, applicants respectfully submit there is no motivation provided within von Behrens or Fite that would direct one of ordinary skill to consider the optical characteristics of their devices. The references are devoid of any suggestion that their device could be used with optical interrogation devices, particularly optical interrogation through the closed end of the container. Accordingly, there is no motivation to combine the teaching of Hawes (relating to laser-excited raman spectrometers) with the teaching of von Behrens and Fite.

Furthermore, applicants respectfully contest the Examiner's assertion that Hawes discloses a capillary tube with a flat end. The reference actually discloses a capillary tube with a convex lens attached to its end. Such additional structure is excluded by applicant narrowly tailored claim. Again, the Examiner is selectively choosing only certain components of a disclosed prior art device for combination with the device of von Behrens without provided legally sufficient grounds for doing so. Applicants note that nowhere within the text of Hawes do the inventors discuss a "capillary tube with a flat tip." The

Appl. No. 09/631,339
Reply to Final Office Action of June 22, 2006

Examiner has failed to explain why one of ordinary skill in the art would be motivated to use a capillary tube with a flat tip in the absence of the convex lens, when removing the convex lens from the device disclosed in Hawes would likely render the device inoperable for its intended purpose. The mere fact that a flat end closed tip may be formed during the process of attaching of a convex lens does not suggest that a capillary tube with a closed end formed as a flat tip is a desirable end product. All the embodiments shown in Hawes include the lens attached to the end of the capillary, and presumably the flat end is required for the attachment of the lens. Accordingly, contrary to the assertion of the Examiner, Hawes does not disclose that it is "conventional" in the art to seal the end of a capillary with a flat tip. Hawes discloses a unique use of a capillary tube where a convex lens needs to be attached to the end of a capillary tube to allow its use with a laser-excited raman spectrometer.

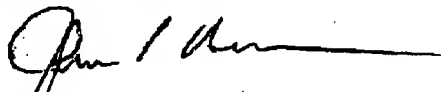
Modifying an element in a prior art reference in a manner that is contrary to its disclosed use cannot serve as the basis of establishing obviousness (see *In re Gordon*, 733 F2d 900 (Fed Cir 1984)). Accordingly, the Hawes reference does not provide motivation to form a container consisting of a receiving portion and a reaction portion, wherein the reaction portion consists of a capillary tube that is closed at one end with a flat tip.

The Examiner notes that the ends of a capillary tube can be sealed separately from the lens as disclosed in Hawes and applicants agree there are many different ways of sealing the ends of a capillary tube. Hawes discloses a manner of sealing a tube so that a convex lens can be attached to the end; there is no suggestion that a capillary tube with only a flat end could be used to allow optical transmissibility through the closed end, as is specifically required in claims 20 and 23. Therefore, the invention of claims 12 and 20 are believed to be patentable over the cited references and applicants respectfully request the withdrawal of the rejection of those claims.

Appl. No. 09/631,339
Reply to Final Office Action of June 22, 2006

The foregoing claim amendments and remarks are believed to fully respond to the Examiner's rejections and the claims are believed to be in condition for allowance. Applicants respectfully request allowance of the claims, and passage of the application to issuance. If any further discussion of this matter would speed prosecution of this application, the Examiner is invited to call the undersigned at (434) 220-2866.

Respectfully submitted,



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